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## IMPACT OF CONCOMITANT AND STAGGERED PANTOPRAZOLE INTAKE ON PHARMACODYNAMIC EFFECTS INDUCED BY CLOPIDOGREL

### i2 Poster Contributions

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**Background:** A pharmacodynamic (PD) drug interaction between proton-pump inhibitors (PPIs), particularly omeprazole, and clopidogrel mediated by the cytochrome P450 (CYP) 2C19 enzyme has been described. However, it is unclear whether this PD interaction is a class-effect or a drug-effect due to controversial results regarding the presence of an interaction with other PPIs which interfere less with the CYP 2C19 enzyme, such as pantoprazole. The aim of this study was to assess the impact of pantoprazole used at high doses on clopidogrel-induced antiplatelet effects.

**Methods:** This was a prospective, randomized, cross-over study conducted in 20 healthy volunteers. Subjects were randomized to receive either clopidogrel 600-mg loading dose (LD) followed by 75-mg maintenance dose (MD) and pantoprazole (80 mg daily). In order to evaluate the impact of timing of administration on PD effects, pantoprazole was administered concomitantly (CONC regimen) or staggered by 8-12 hours (STAG regimen) for 1 week in a cross-over fashion with a 2-4 week washout between treatment periods. After another washout period, subjects were treated for 1 week with clopidogrel only (CLOP regimen). Platelet function was assessed by flow cytometric analysis of VASP-P, light transmittance aggregometry (LTA) following ADP stimuli and VerifyNow P2Y12 system at 3 time-points: baseline, 24 hours post LD and 1 week post-MD. The primary endpoint was the comparison of P2Y12 reactivity index (PRI) assessed by VASP-P at 1 week. Values are expressed as LS mean [95% confidence interval].

**Results:** Similar PRI values were obtained with the CONC and STAG regimens after 1 week of treatment (56.0 [48.0-64.1] vs. 56.1 [48.1-64.2];  $p=ns$ ). Further, no significant difference was observed in PRI values achieved with the CLOP regimen (61.0 [52.9-69.0]) when compared with the CONC ( $p=ns$ ) and STAG ( $p=ns$ ) regimens. No differences were observed at baseline and 24 hours between regimens. Concordant results were obtained by LTA and VerifyNow P2Y12 testing.

**Conclusions:** Pantoprazole used at high doses does not affect clopidogrel-induced antiplatelet effects, irrespective of regimen of administration (concomitant or staggered) used.